WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2005/050273

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-9
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-9
Industrial applicability (IA)	Yes:	Claims	1-9
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

D1: WO 02/40007 A (NOVARTIS AG; NOVARTIS-ERFINDUNGEN VERWALTUNGSGESELLSCHAFT M.B.H; HEWIT) 23 May 2002 (2002-05-23)

D2: RADDATZ P ET AL: "RENIN INHIBITORS CONTAINING NEW P1-P1' DIPEPTIDE MIMETICS WITH HETEROCYCLES IN P1'" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 35, no. 19, 18 September 1992 (1992-09-18), pages 3525-3536, XP002050635 ISSN: 0022-2623

D3: ALLIKMETS K: "ALISKIREN SPEEDEL" CURRENT OPINION IN INVESTIGATIONAL DRUGS, PHARMAPRESS, US, vol. 3, no. 10, 2002, pages 1479-1482, XP009017210 ISSN: 1472-4472

D4: WOOD J M ET AL: "Structure-based design of aliskiren, a novel orally effective renin inhibitor" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, ACADEMIC PRESS INC. ORLANDO, FL, US, vol. 308, no. 4, 5 September 2003 (2003-09-05), pages 698-705, XP004447169 ISSN: 0006-291X

1. The present application relates to amino alcohols (I), (Ia), (Ib), (Ic) and (Id); pharmaceutical preparation comprising them and their use in the preparation of pharmaceutical compositions having renin-inhibition action.

2. D1-D4 disclose amino alcohols useful in the treatment of renin-inhibition related diseases.

Novelty

3. The subject-matter of claims 1-9 is novel in the sense of Art. 33(2) PCT. None of the available documents of the prior art discloses compounds of formulae (I), (Ia), (Ib), (Ic) and (Id). The present claimed compounds differ from those known in the prior art in the relative position of the amino and alcohol groups. Hence, the use of the present claimed

compounds in the treatment of renin-inhibition related diseases is novel as well.

Inventive step

4. The subject-matter of claims 1-9 cannot be considered to involve an inventive step in the sense of Art. 33(3) PCT.

Due to the facts that a)in all the prepared compounds R_6 is CO; both R_5 together are isopropyl; R_3 and R_4 are hydrogen and R is a 1,2,3,4-tetrahydro-quinolin-carbamic acid methyl ester and furthermore b)in view of not having activity data providing an indication of which compounds have been found active, there is no evidence of the activity of the present claimed compounds. Hence, there is no proof of having solved the technical problem of providing renin inhibitors and therefore, an inventive step cannot be acknowledged. Inventive step can only be acknowledged if activity data are provided showing which compounds have been found active and inventive activity would only be acknowledged for a scope of compounds covered by the data provided. Hence, if data is only provided for the compounds prepared in the description, then the claims should encompass only compounds with R_6 =CO; both R_5 together =isopropyl; R_3 and R_4 =hydrogen and R = 1,2,3,4-tetrahydro-quinolin-carbamic acid methyl ester.

Further comments

5. The term "prodrug" used in claims 1, 2 and in the description renders unclear the scope of the protection sought, contrary to Art. 6 PCT. This term should not have been used in drafting the description and the claims.

6. The term "lower" (alkyl, alkoxy,...) has no generally accepted meaning in the art (see Decision T 337/95 of the EPO Boards of Appeal) and is regarded as unclear, since the higher limit of carbon atoms is not unambiguously defined (Art. 6 PCT). Claims 1 and 2 should have been drafted with the definition of this term in the application according to lines 1 and 2 at page 3 in the description and not including this term.

6. Features introduced by terms like "such as", "for example" and "in particular" have no limiting effect on the scope of the claim including them (see PCT Guidelines, C-III, 4.6).

The presence of such non-limiting features is however detrimental to the conciseness of claims 3-6, contrary to Art. 6 PCT.

7. The second paragraph on page 5 is vague and imprecise, rendering therefore unclear the scope of the protection sought, contrary to Art. 6 PCT. This paragraph should not have been introduced in the description.

8. The use of the word "about", especially in connection with numerical ranges, is generally regarded as rendering the determination of the exact scope of the range difficult. When used in a claim as well as in the description, this results in lack of clarity, contrary to Art. 6 PCT. Therefore, the description should not have been drafted using this word.

9. The use of the word "etc." in the description renders unclear the scope of the protection sought, contrary to Art. 6 PCT.

10. When filing amended claims the applicant should at the same time bring the description into conformity with the amended claims.

11. In order to facilitate the examination of the conformity of the amended application with the requirements of Article 19 (2) and 34(2)b) PCT, the applicant is requested to clearly identify the amendments carried out, irrespective of whether they concern amendments by addition, replacement or deletion, and to indicate the passages of the application as filed on which these amendments are based.

If the applicant regards it as appropriate these indications could be submitted in handwritten form on a copy of the relevant parts of the application as filed.